SUPPORT FOR THE AMENDMENTS

Claims 1-5 have been amended.

Claims 6-11 have been added.

Support for the amendment of Claims 1-5 is provided by originally filed Claims 1-5.

Support for new Claims 6-11 is provided by page 4 of the specification.

No new matter is believed to be entered by the present amendments.

REMARKS

Claims 1-11 are pending in the present application.

The rejection of Claims 1-5 under 35 U.S.C. §103(a) over US 5,545,755 (Lin et al) and US 4,640,921 (Othmer et al) in view Rehman et al is respectfully traversed.

The claimed invention relates to a method of treatment of sexual dysfunction by administering to a person in need of treatment an effective amount of gepirone as either a short-term or a long-term therapy, wherein said sexual dysfunction is a sexual disorder selected from the group consisting of hypoactive sexual desire disorder, orgasmic disorder, and sexual arousal disorder. Applicants submit that the art of record does not support a conclusion of obviousness.

The Examiner alleges that Lin et al disclose that 5HT-1A agonists are useful in treating sexual dysfunction and that gepirone is a 5HT-1A agonist. Although it is true that gepirone is a 5HT-1A agonist, the Examiner's characterization of the role of 5HT-1A agonists in treating sexual dysfunction is not accurate. At column 1, lines 53-55, Lin et al disclose:

> "5HT-1A agonists ***may be useful*** in treating overeating and sexual dysfunction. These compounds have been shown to alter feeding and sexual behavior in animals." (***emphasis added***)

Applicants submit that Lin et al merely speculates on a possible role (i.e., "may be useful"), but offers no evidence or technical basis to conclude that 5HT-1A agonists in general, much less gepirone specifically, actually do treat sexual dysfunction.

Indeed, the Examiner cites Rehman et al, which directly contradicts the Examiner's allegations. In the Abstract, Rehman et al disclose:

> "the effects of buspirone (2 mg/kg) and gepirone (2 mg/kg) on copulatory behavior were ***indistinguishable*** from control." (***emphasis added***)

Further, bridging pages 417-418 and in Figures 3-4, Rehman et al clearly show that copulatory behavior based on frequency of intromission, latency (intromission, of ejaculation, and post-ejaculation), frequency of mounts, intromission, and ejaculation per 20 minutes, is at best unaffected and in most cases is actually *inhibited* by administration of 2 mg/kg of gepirone. Rehman et al also reference on page 418, left column, lines 9-11 a "typical '5-HT behavioral syndrome'" that was "consistently observed in which the rats' copulatory behavior was partially inhibited". Accordingly, Rehman et al may disclose modulation of sexual behavior, but this is not treatment as is presently claimed but rather would inhibition. Thus, Rehman et al clearly defeat the Examiner's alleged obviousness as Applicants remind the Examiner that MPEP §2141.02 states: "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

With respect to Othmer et al, this reference only relates to buspirone. At no point does Othmer et al, Lin et al, or especially Rehman et al, provide any disclosure or suggestion that the results obtained for buspirone would be applicable to gepirone. Indeed, buspirone and gepirone are both considered to be 5HT-1A agonists, but this is where the comparison ends.

Specifically, buspirone and gepirone are not "chemically similar." The structure of busprione has been studied with respect to the dopamine (D-2) receptor binding activity and it was speculated that the critical determinant for dopamine receptor binding was the interaction between a lipophilic site on the receptor and the azaspirodecanedione moiety of buspirone. Accordingly, the azaspirodecanedione moiety or buspirone was modified with a gem-dimethyl moiety resulting in the loss of dopamine binding activity and the creation of gepirone.

In gepirone, it is well established that the gem-dimethyl moiety replacement not only resulted in 5-HT1A receptor binding activity being retained, but resulted in a significant increase in the agonist character resulting from this binding was observed as compared to the weak 5-HT1A partial agonist character of buspirone. Therefore, buspirone and gepirone are distinct from a chemical *and* receptorological standpoint. Specifically, buspirone and gepirone are structurally distinct and, thus, possess differing receptor binding preferences (i.e., buspirone is a D-2 antagonist/5-HT1A *partial* agonist, whereas gepirone is a 5-HT1A agonist).

In view of the structural (azaspirodecanedione moiety versus a gem-dimethyl moiety) and receptorological differences between buspirone (D-2 antagonist/5-HT1A partial agonist) and gepirone (5-HT1A agonist), no chemical basis exists to lead the artisan to expect the effect disclosed in Othmer et al for buspirone could be extended to gepirone especially in view of the disclosure of Rehman et al.

In view of the foregoing, Applicants request withdrawal of this ground of rejection.

The objection to Claims 2 and 3 is obviated by amendment. Applicants have amended Claims 2 and 3 to remove the parenthetical phrase. Withdrawal of this ground of objection is requested.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

Richard D. Kelly
Attorney of Record
Registration No. 27,757

Vincent K. Shier, Ph.D.
Registration No. 50,552

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413-2220
(OSMMN 08/03)